HIV False Negative case

IVD International Clinical Application Department

Sang

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Case Background

Background

A private labs had a concern was about HIV result for a patient who was sent back because of HIV Ab/Ag positive, and on returning to diagnostic a rapid testing with determine kit and A Brand was positive.

Mindray CL-1200i initial and repeat results were both negative.

Mindray CL-1200i: 0.1 Negative

Determine Alere Rapid Test: Positive

A Brand: 5.74 Positive

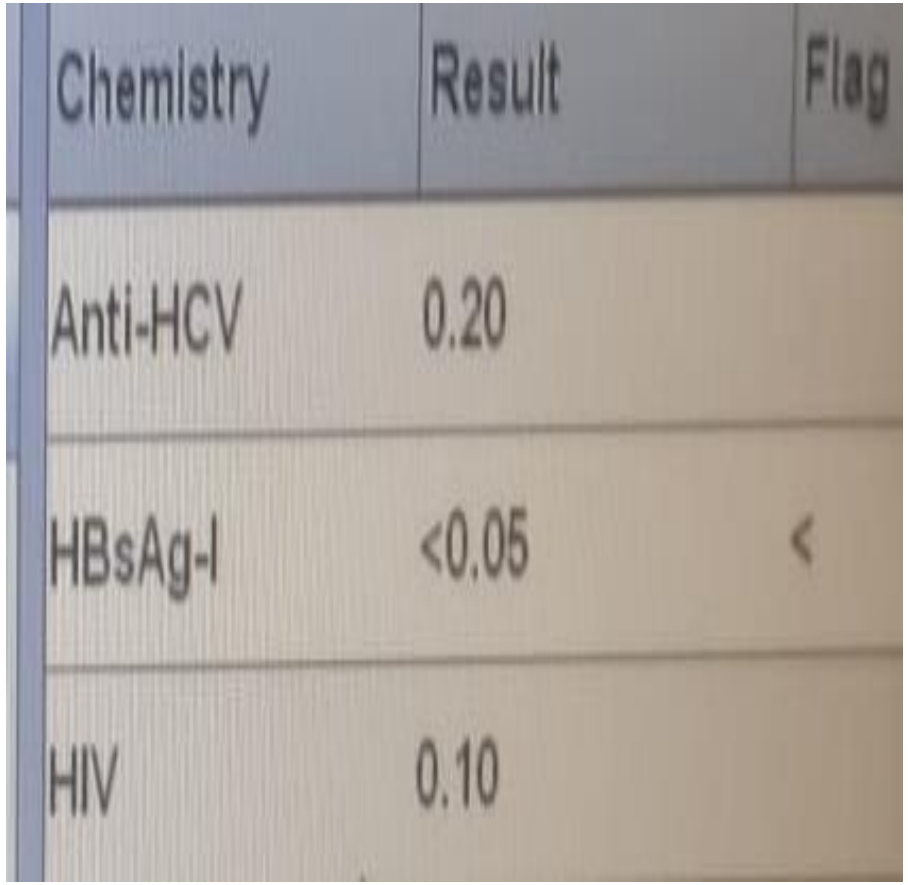
Complain

The customers complain about the Mindray results do not correlate with other platforms. The false Negative would result to the laboratory being fined or with increased number leads to license cancellation.

Expectation

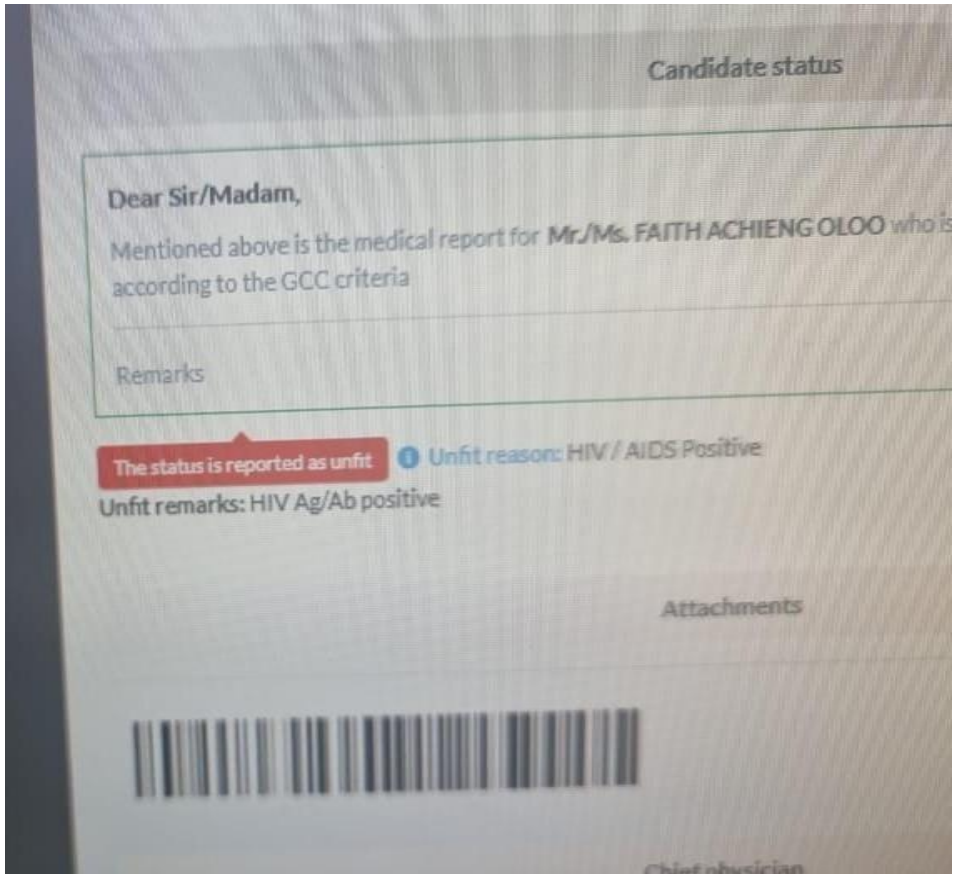
The customer was very angry about false positive of HIV, they need Mindray to find out the root cause of this issue.

Case Background



Mindray result HIV Ab/Ag non-reactive

RDT determine results HIV Negative



GCC results HIV Ab/Ag positive

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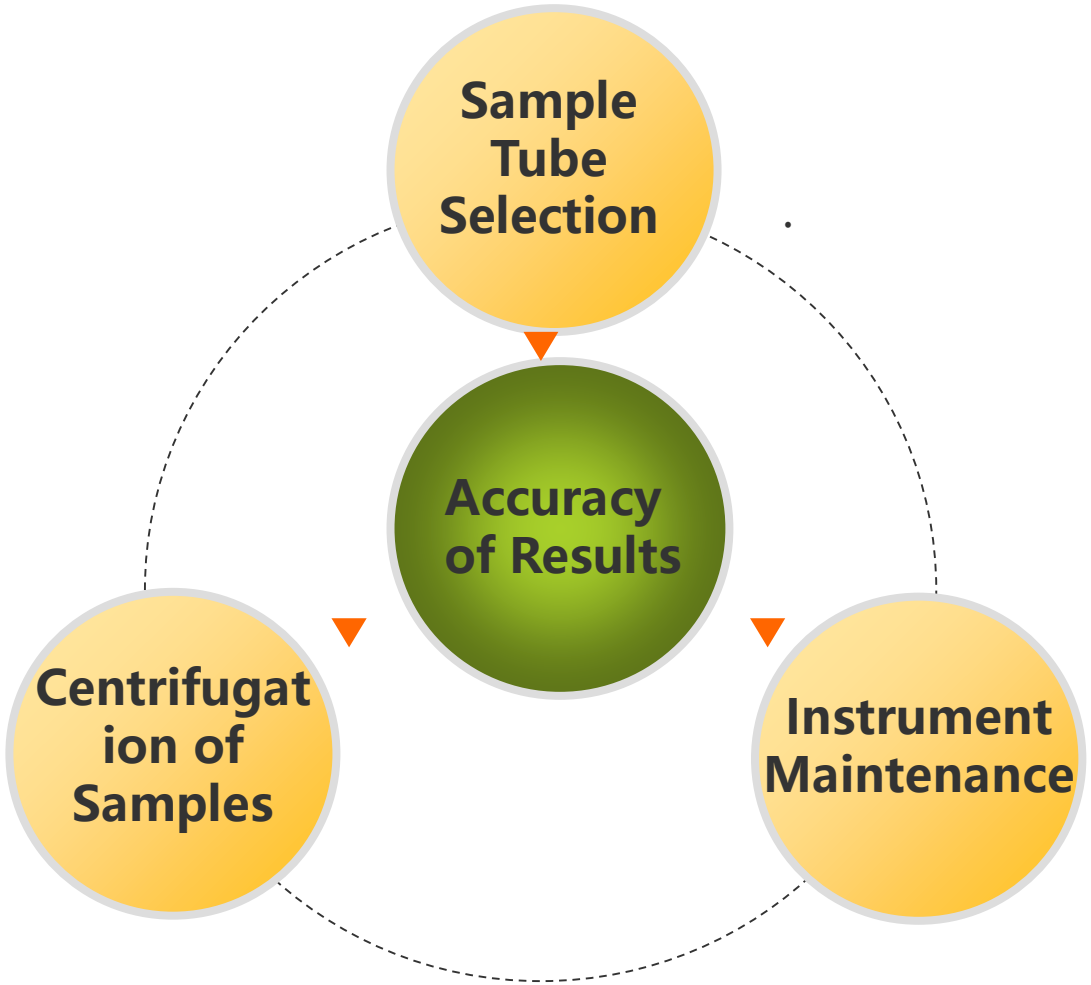
Test quality results indicators



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Case Ideas

Verify the preanalytical and sample pretreatment protocol

	Bayan lab
Syringe	BD
Needle	BD
Agglutination	>30min
Centrifuge	4000RPM, 10min
Pipette used to Transfer serum to Sample Cup	Yes
Sample Cup	biosystem
Retest Procedure	Retest the positive samples after re-centrifugation, if it's still positive recollect the sample after two weeks and retest. Send the repeatedly positive samples out for confirmation.
Reagent/calibration storage	2-8 c and monitored daily

Reagent storage & lab environment were normal.

Sample pretreatment is normal.

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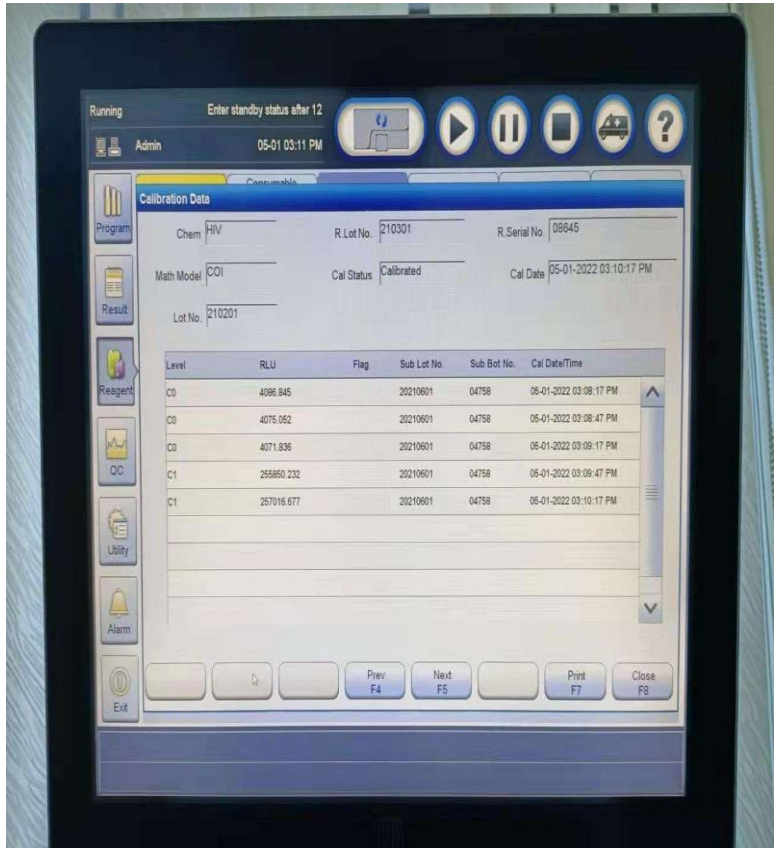
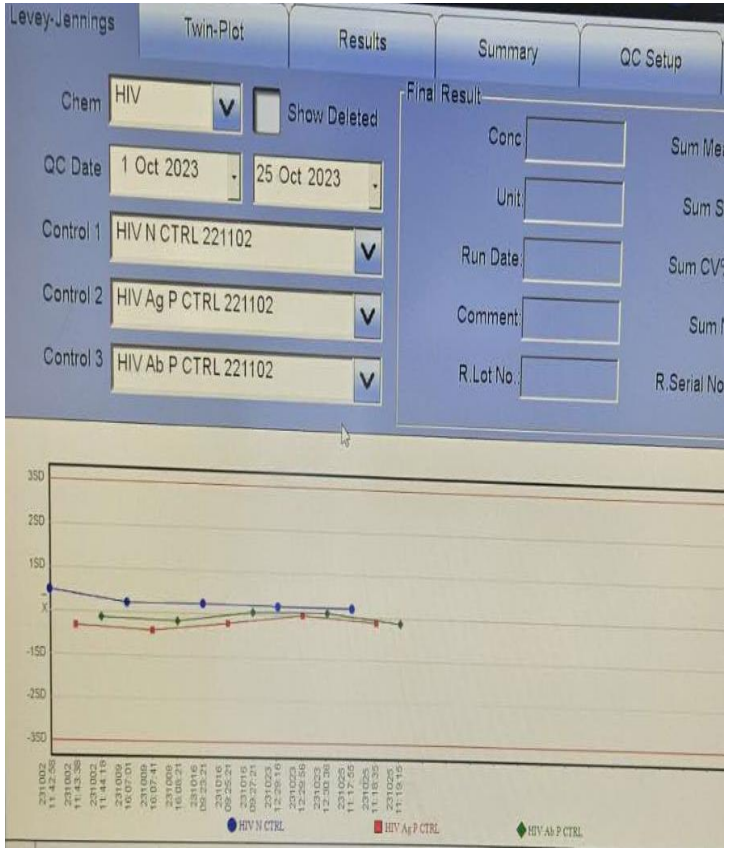
Case Ideas

Verify the analytical aspects





Basic Check:

Calibration and QC results were normal, the sample was rerun on Mindray, and the result was the same. Serum was clear without foreign body. Patient denied any medicine or exposure history.

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Case Ideas

Possible Reasons Causing false negative for Mindray

- Individual is in the eclipse period before detection of Ag or HIV RNA possible;
- Individual is in acute phase of infection (before seroconversion) but is screened using a less sensitive method that detects Abs only;
- Individual in the early stage of seroconversion but is screened using a less sensitive method that does not detect early (IgM) Abs;
- Technical errors;
- Other core possibilities:
  - ✓ Delayed Ab synthesis in infants and persons receiving PEP or PrEP or who have concurrent acute hepatitis C infection;
  - ✓ Diminished immune response in individuals receiving intensive or long-term immunosuppressive therapy;
  - ✓ Congenital or drug-inducted hypogammaglobulinemia or agammaglobulinemia;
  - ✓ Insufficient host Ab response (i.e., advanced HIV disease)
  - ✓ Unavailability of Abs due to the formation of Ag-Ab complexes

Case Ideas

Possible Reasons Causing false positive for A Brand and RDT

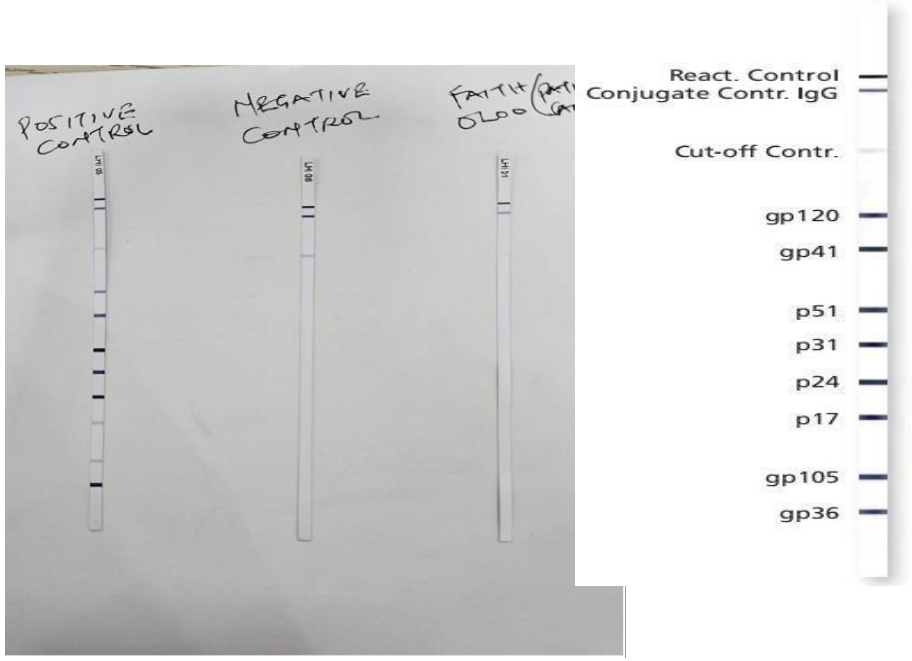
- Increased sensitivity of assays, leading to reduced specificity;
- Technical errors (specimen mix-up, mislabeling, improper handling);
- Presence of HIV Abs in recipients of HIV-1 trial vaccines;
- Other rare possibilities:
  - ✓ Hypergammaglobulinemia/Abs reactive to cellular components;
  - ✓ Influenza vaccination may cause cross-reactivity with HIV Ab assay. The time course for such cross-reactivity remains uncertain;
  - ✓ Autoimmune disorders and other medical conditions;
  - ✓ Multiple transfusions

Case Solution

Troubleshooting:

Confirmation tests of HIV are PCR test and western blotting:

- The sample was sent to be tested for HIV-1, the result was negative.
- Western blotting reagent was sent to the customer side, it turns out the sample was negative on both HIV-1 and HIV-2.



The *recomline* HIV-1 and HIV-2 IgG is a qualitative test for detection of IgG antibodies against specific antigens. By using the type-specific antigens gp41(HIV-1) and gp36(HIV-2) making it possible to differentiate between an infection with HIV-1 and HIV-2.

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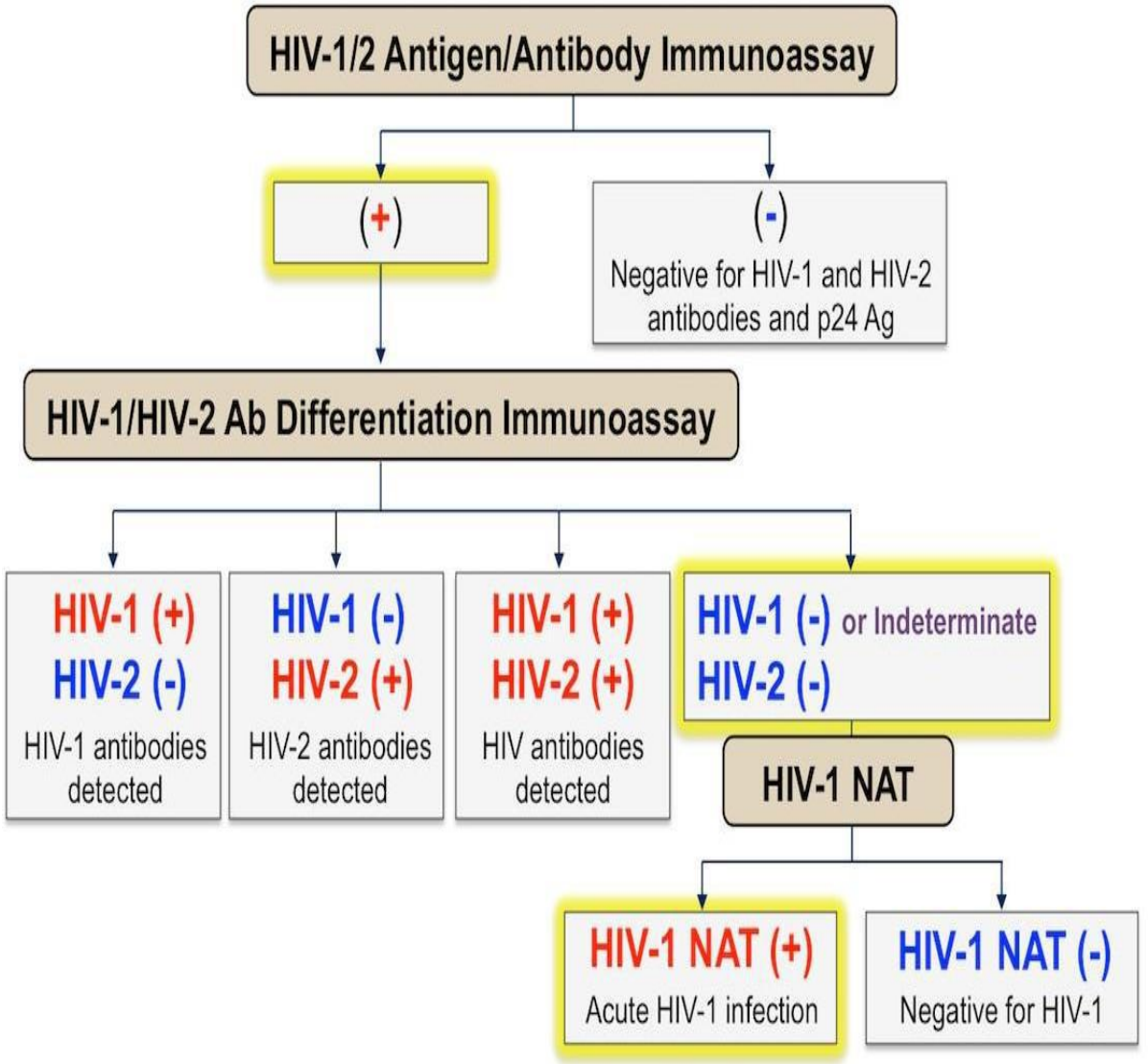
Case Solution

- According to researches, HIV-2 was only popular in some areas, for the rest of the world, HIV-1 is more popular.

Conclusion:

- It was not Mindray who gave false negative result, it was the rapid test and A Brand reagent that gave false positive result.
- CDC HIV diagnosis procedure should be applied in the customer side to avoid false results.



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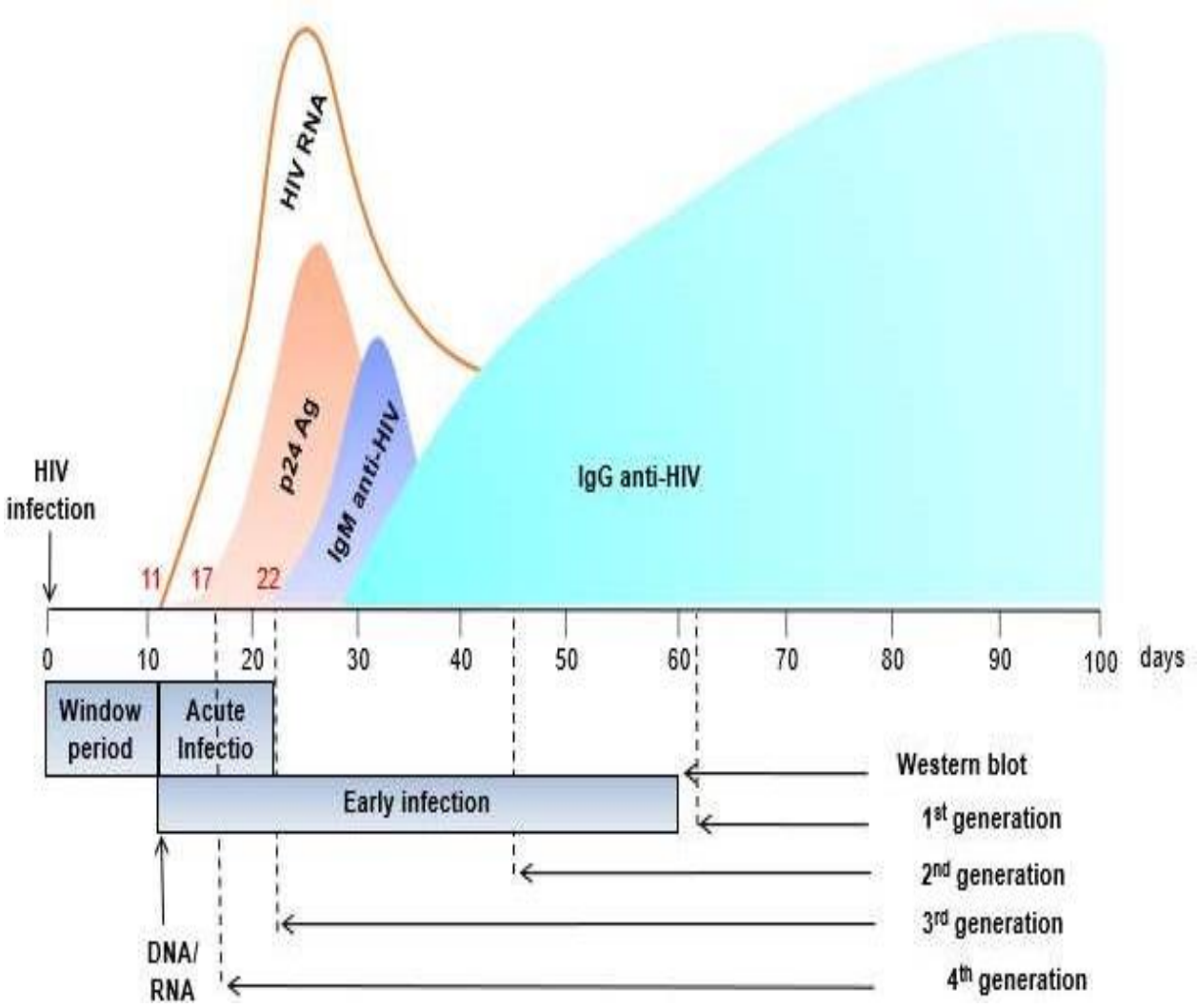
Case Summary



As we all known, HIV kit is the 4th generation which shorten to around 2 weeks for HIV detection, Mindray HIV kit is also the 4th generation which added the p24 antigen so that the window period can be shortened to fourteen daysto improve the early detection capability.

Incase of new HIV mutation could be generated, which is not sensitive to HIV kit. Antibody sensitivity of Mindray is not enough for HIV infection screening, the performance evaluation indicates that The Mindray Antigen and Antibodies to Human deficiency Virus (CLIA) test had a specificity of 99.5% and sensitivity of 100% for HIV-1 and HIV-2 blood samples,

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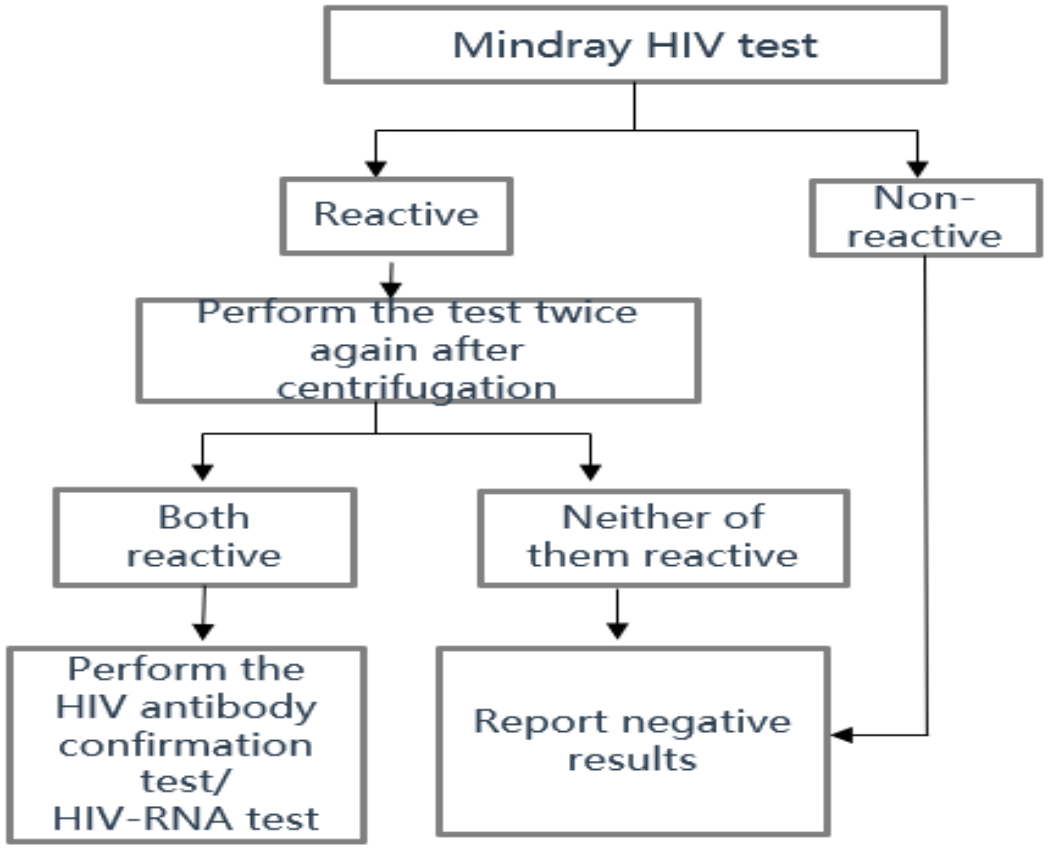
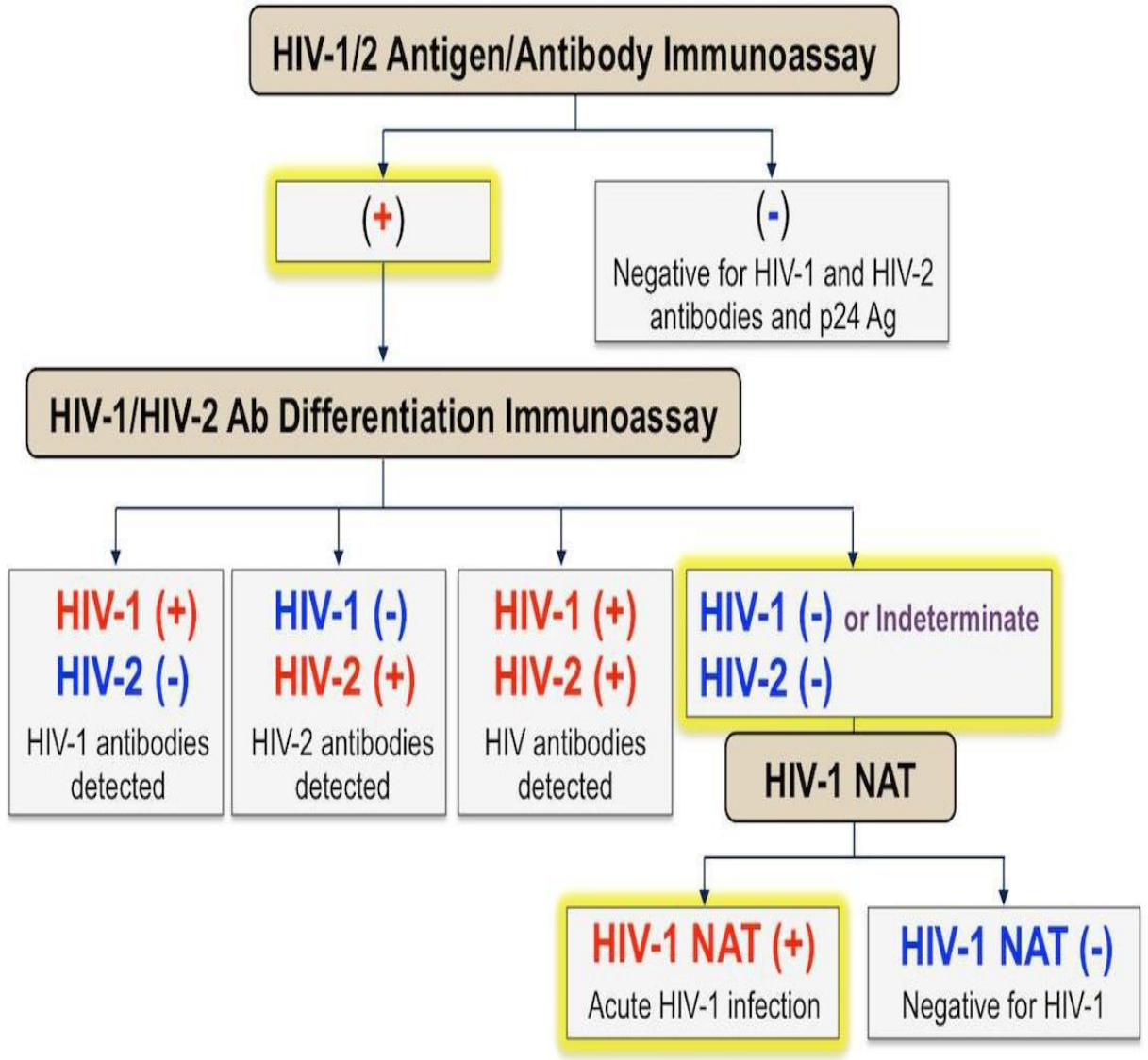
Case Summary





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Thanks!

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